Exhibit A

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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/824,075	04/14/2004	Mary E. Gerritsen	P2014R1	7011

9157 7590 10/23/2007

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EXAMINER	
LI, RUIXIANG	

ART UNIT	PAPER NUMBER
1646	

MAIL DATE	DELIVERY MODE
10/23/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/824,075	GERRITSEN ET AL.	
	Examiner	Art Unit	
	Ruixiang Li	1646	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *10 August 2007*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *13-20* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *13-20* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *08/10/2007*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Status of Application, Amendments, and/or Claims

Applicants' amendment filed on 08/10/2007 has been entered in full. Claims 13 and 18-20 are amended. Claims 13-20 are pending and under consideration.

Withdrawn Objections and/or Rejections

The rejection of claims 13-20 under 35 U.S.C. 112, second paragraph is withdrawn in view of amended claim 13.

The objection to claims 13, 19, and 20 is withdrawn in view of the amended claims.

Information Disclosure Statement

The information disclosure statement filed on 08/10/2007 has been considered by the examiner.

Claim Rejections under 35 USC § 112, 1st paragraph

(i). The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

(ii). The rejection of claims 13-20 under 35 U.S.C. 112, first paragraph, for written description is maintained.

At page 5, 1st paragraph of Applicants' response, Applicants review the legal standard for written description, with which the examiner does not take an issue.

At page 5, 2nd paragraph of Applicants' response, Applicants argue that Applicants have adequate written support throughout the specification for the disclosed method. This is not found to be persuasive because the issue here is not whether the specification provides "literal" support for the claimed invention; instead, it is whether the specification meets the written description requirement.

Beginning at page 5, 3rd paragraph of Applicants' response, Applicants argue that Applicants teach the activities in the Matrigel and migration assay, which are well accepted in the art as models for the multi-staged angiogenesis process, provide unexpected and important evidence for a role for stanniocacin in vascularization and angiogenesis-associated signaling and function. Applicants also argue that in the context of describing the role of STC-1 in various stages of angiogenesis, Applicants teach that these effects were selective to particular angiogenic factors, in particular HGF, because the responses of endothelial cells to either VEGF or bFGF were not modulated in these assays.

Applicants' argument has been fully considered, but is not deemed to be persuasive for the following reasons. The specification discloses that human STC-1 inhibits migration of human umbilical vein endothelial cells (HUVECs) induced by HGF (Fig. 2, page 55 of

the specification) and reduces endothelial cord formation on Matrigel induced by 20 ng/ml HGF (Fig. 4, page 56 of the specification), but has no effect on migration of HUVECs induced by bFGF or VEGF and on proliferation of HUVECs stimulated by HGF (10 ng/ml), bFGF (10 ng/ml), and VEGF (10 ng/ml) (page 55 of the specification). However, there is no disclosure of any other angiogenic factors or any other type of cells; there is no evidence showing that human STC-1 has no effect on bFGF or VEGF-induced angiogenesis that involves multi-stages. More importantly, there is no showing that STC-1 inhibits any step of the angiogenic process of a cell promoted by HGF but not bFGF or VEGF when the cell was exposed to both HGF and bFGF (or VEGF), needless to say any other angiogenic factors. Thus, the specification fails to provide adequate written description for the instantly claimed invention.

Beginning at page 7, 4th paragraph of Applicants' response, Applicants argue that Applicants clearly teach functional features as well as structural features of STC-1 (SEQ ID NO:2) or a variant thereof. Applicants also argue that Applicants teach various assays for relevant functional activity generally throughout the specification. Applicants further argue that Applicants teach homologues (STC-2) and orthologues (fish) for structural context.

Applicants' argument has been fully considered, but is not deemed to be persuasive for the following reasons. First, a biomolecule described only by a functional characteristic, without any known or disclosed correlation between that function and the structure of

the biomolecule, normally is not a sufficient identifying characteristic for written description purposes because a functional activity only indicates what a compound, does not indicate what a compound is.

Second, with respect to the use of an assay to support written description, in *University of Rochester*, the patent claimed a method of selectively inhibiting the enzyme PGHS-2 (also known as COX-2) by "administering a non-steroidal compound that selectively inhibits activity of the PGHS-2 gene product in a human." *Id.* at 918, 69 USPQ2d at 1888. The patent "described in detail how to make cells that express either COX-1 or COX-2, but not both..., as well as 'assays for screening compounds, including peptides, polynucleotides, and small organic molecules to identify those that inhibit the expression or activity of the PGHS-2 gene product.[']" *Id.* at 927, 69 USPQ2d at 1895.

The court held that the disclosure of screening assays and general classes of compounds was not adequate to describe compounds having the desired activity: without disclosure of which peptides, polynucleotides, or small organic molecules have the desired characteristic, the claim failed to meet the description requirement of §112. See id. ("As pointed out by the district court, the '850 patent does not disclose just 'which "polypeptides, polynucleotides, and small organic molecules" have the desired characteristic of selectively inhibiting PGHS-2.'...Without such disclosure, the claimed methods cannot be said to have been described.").

Third, the claims do not require that the STC-1 variant possess any particular conserved structure nor disclosed distinguishing feature. The instant disclosure of a human STC-1 polypeptide set forth in SEQ ID NO: 2 does not adequately support the scope of the recited genus, which encompasses a substantial variety of homologues or variants of the STC-1 polypeptide of SEQ ID NO: 2. STC-2 and orthologues (fish) are not considered as a STC variant in the instant specification because they do not have at least about 80% amino acid sequence identity with human STC-1 of SEQ ID NO: 2 (see page 8, lines 21-25; page 57, lines 6-8).

Moreover, the specification does not provide any structural characteristics to adequately describe the genus of STC-1 variants that may be administered in the claimed method. There is no defined relation between function and structure of the STC-1 variants. There is even no identification of any particular portion of the structure that must be conserved.

Finally, the prior art does not provide compensatory teachings to enable one skilled in the art to recognize that Applicant was in possession of the genus of STC-1 variants and thus instantly claimed methods. Accordingly, one skilled in the art would not recognize from the disclosure that the Applicants were in possession of the claimed methods at the time the application was filed.

Conclusion

No claims are allowed.

THIS ACTION IS MADE FINAL. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ruixiang Li whose telephone number is (571) 272-0875. The examiner can normally be reached on Monday through Friday from 8:30 am to 5:00 pm. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Nickol, can be reached on (571) 272-0835. The fax number for the organization where this application or proceeding is assigned is (571) 273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, please contact the Electronic Business Center (EBC) at the toll-free phone number 866-217-9197.

Ruixiang Li

Ruixiang Li, Ph.D.
Primary Examiner
October 16, 2007

RUIXIANG LI, PH.D.
PRIMARY EXAMINER